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8-Methoxypsoralen Acts on Lymphocyte Membranes in the Dark

To the Editor:

With great interest we have read the article by Dr. Malinin et al, "Ultrastructural modifications of the plasma membrane in HUT 102 lymphoblasts by long-wave ultraviolet light, psoralen, and PUVA" (J Invest Dermatol 95:97–103, 1990). The authors described therein membrane alterations after incubation of the cells with a suprapharmacologic concentration of the photosensitizer 8-methoxypsoralen (8-MOP) in the dark and suggest that cell membrane components are the primary target in the 8-MOP action mechanism.

The dark effect of 8-MOP on lymphocyte surface structures has been well documented by ourselves and others in several investigations using different methods with regard to their membrane-related evidence. Among other things, it has been shown that, following high dosages of 8-MOP, parts of the glycocalyx [1] and the cytoplasm [2] were released from leucocytes and lymphocytes, respectively, into the medium under cell culture conditions. However, morphologic changes could not be observed under the influence of 8-MOP in therapeutic concentrations [3]. On the other hand, without any UV-irradiation 8-MOP was able to increase the membrane-associated cAMP levels in mononuclear leucocytes [4], possibly by inhibition of phosphodiesterase [5] after only 1 min incubation time. Furthermore 8-MOP has shown to inhibit both the PHA and Con A–induced proliferation of normal human peripheral blood lymphocytes in a time- and dose-dependent manner [6,7]. This was explained by the decrease in IL-2 receptor expression on PHA-stimulated lymphocytes [6]. As we have shown, the PHA-triggered cytokine release (macrophage slowing factor [8]) and the HLA-DR expression [7] were depressed by 8-MOP, too. In addition, 8-MOP was able to temporarily reduce the binding of sheep erythrocytes to lymphocytes, which is known as membrane interaction [7]. Finally, 8-MOP reduced the number of Pan T cells evaluated by specific monoclonal antibodies [9].

Taken together, 8-MOP exerts some dark effects on lymphocyte surface membranes. These results may suggest some immunoregulatory effects of 8-MOP on (antigen activated) cells. Because of their only slight degree and transient nature [4,6–9], these 8-MOP dark effects are probably of low clinical relevance under therapeutic conditions.

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REPLY

In their letter concerning our article [1], Drs. Gast and Haustein note, firstly, that "dark effect of 8-MOP on lymphocyte surface structures is well documented," and secondly conclude that "because of their only slight degree and transient nature these 8-MOP dark effects are probably of low clinical relevance."

We agree with the authors that dark 8-MOP reaction with lymphocytes and, with other cells, was indeed documented [2]; however, the availability of diverse phenomenologic data does not automatically imply understanding of underlying reaction mechanisms, and their biologic significance. Because photoreactions of 8-MOP, at least in part, are preceded and facilitated by dark reactions with specific targets, their ultimate significance cannot be extrapolated solely on the basis of their transience or detection by a single method.